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PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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London WC1X 8BT
GRANDE BRETAGNE

PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	06.10.2003
Applicant's or agent's file reference: SJA/59666/001	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB02/04489	03.10.2002	10.10.2001

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68

Applicant
MICROSENS BIOPHAGE LIMITED

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 10.02.2004

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10 OCT 2003

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I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-38 as originally filed

Claims, Numbers

1-44 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this opinion.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1, 2, 31, 32, 42 and related claims

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1, 2, 31, 32, 42 and related claims

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	
Inventive step (IS)	Claims	1-7 15-21 25-28 31-36 39 42-44
Industrial applicability (IA)	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

As outlined in the International Search Report (ISR) the search for **claims 1, 2, 31, 32, 42** and related claims has been restricted to subject-matter which appeared to be supported and disclosed (see ISR, PCT/ISA form 210), i.e. the subject-matter of claim 3, i.e. methods wherein the interaction between nucleic acid moieties occurs by recombination.

The International Examination Authority (IEA) fully supports the objections made in the ISR.

The Applicants attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The Applicant is advised that the EPO cannot normally carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any international Preliminary Examination procedure.

As a consequence, the present examination only relates to the searched subject-matter as identified above.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. **Reference** is made to the following documents:

   D1: WO 97 00446 A (LANDEGREN ULF) 3 January 1997
   D2: KIM H-S ET AL: NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 16, no. 18, 1988, pages 8887-8903,
   D3: WO 90 11375 A (DU PONT) 4 October 1990,
   D4: WO 01 61037 A (FREDRIKSSON SIMON ;LANDEGREN ULF (SE)) 23 August 2001.

2. **Clarity, Support and Disclosure** (Articles 5 and 6 PCT):

2.1 Since recombination is a form of covalent cross-linking, the subject-matter of **claims 3-5** and claims dependent thereof, as well as the embodiments described on pages 25-28 and the examples, do not fall under the scope of claims 1, 2, 31, 32 and 42.

2.2 In addition to the objections made under item III above, it should be noted that no enabling examples has been given for the subject-matter of **claims 8-14, 22-24, 29, 30, 37, 38, 40 and 41**. Since these embodiments are not trivial, i.e. cannot be carried out by the skilled persons without using inventive skill, these claims lack support and disclosure.

3. **Inventive step** (Article 33(3) PCT):

3.1 Document D1, which represents the closest prior art, discloses (see abstract and pages 3-6) a method for the detection of a target molecule wherein the sample is contacted with binding moieties having nucleic acid tags. If binding with the target occurs, the tags interact and are covalently cross-linked by ligation to form an amplicon, which can be detected by PCR.
The distinguishing feature between D1 and the subject-matter of claim 1 is that the formation of the amplicon is the result of an recombination event.
Since this distinguishing feature has no technical effect, since with both methods an amplicon is formed, the method disclosed in D1 and the method of the present invention are alternatives.
Thus the objective technical problem underlying the claimed subject-matter with regard to D1 can be defined as finding an alternative method to generate an detectable amplicon upon interaction between two nucleic acid tags.
Document D2 discloses a method for the detection of recombination events wherein desired recombination events result in the formation of an amplicon.
Thus, it would be obvious to the person skilled in the art, namely when the same result is to be achieved, to combine the methods of D1 and D2 in order to arrive at the subject-matter of claims 1-5, 31- 35, 42 and 44.
The subject-matter of **claim 1-5, 31- 35, 42 and 44** does therefore not involve an inventive step.

3.2 As the features of **claims 6, 7, 15-21, 25-28, 36 and 43** are described in documents D1-D4 as providing the same advantages as in the present application, these claims are not inventive either.